

REMARKS

Applicants and their undersigned representative respectfully acknowledge the time and courtesy accorded them by the Examiners, Mr. Kishore and Mr. Oh, during the Interview conducted on October 20, 2005. A summary of the substance of the Interview is included in the above amendments and the following remarks.

The Amendments

The claims are presented as a new claim set but are directed to subject matter of the same nature as the previous method claims 162-187. Pursuant to the discussion at the Interview, the new claims have been written to clarify certain aspects of the invention. All the claims are now method claims directed to suppressing spermatogenesis, inducing azospermia and/or inducing oligospermia in a male. This recitation is supported by the disclosure at page 1, lines 7-10, page 3, lines 10-12 and 32-34, page 4, lines 1-12, and page 9, lines 14-19, for example. During the Interview, the examiner's indicated that this language more clearly defined the method. The new claims further recite that the testosterone ester is administered by intramuscular injection, subcutaneous implantation, or subcutaneous injection. This recitation is supported by the disclosure at page 17, lines 6-14, for example, including the feature that the testosterone ester and the norethisterone may be separately administered by different mode of administration. This recitation addresses the discussion at the Interview that the claims would be further distinct from the prior art (see below) where the particular mode of administration is recited. The claims also specify the manner of derivatives of the norethisterone, as supported at page 4, lines 18-26, for example, and the type of androgen, as supported at page 17, line 33, to page 18, line 2, for example. It was

discussed at the Interview that this added to the definiteness of the claims to make the distinction from the prior art more clear.

To the extent that the amendments avoid the prior art or for other reasons related to patentability, competitors are warned that the amendments are not intended to and do not limit the scope of equivalents which may be asserted on subject matter outside the literal scope of any patented claims but not anticipated or rendered obvious by the prior art or otherwise unpatentable to applicants. Applicants reserve the right to file one or more continuing and/or divisional applications directed to any subject matter disclosed in the application which has been canceled by any of the above amendments.

The Rejection under 35 U.S.C. §103

The rejection of claims 130-138, 143-154, 158-170, 172, 173 and 175-187 under 35 U.S.C. §103, as being obvious over Guerin (Intl. J. Andrology), is respectfully traversed.

The discussion of Guerin in the Reply filed February 5, 2004, still applies and is incorporated herein by reference. The following comments are provided for emphasis purposes and/or to summarize the Interview.

Guerin teaches, as its contribution, three specific regimens for daily administration of hormones for male contraception. In all three regimens, the progestagen (e.g., norethisterone acetate) is administered orally. Guerin also discusses what was allegedly done before their contribution in the section entitled "Introduction" at the first and second pages. It is alleged in the Office Action that this Introduction section of Guerin teaches that "both steroid classes [progestagens and androgens] are generally administered by intramuscular injections." Guerin cited five articles as supporting such a broad statement. These actual articles, in fact, do not support such a broad teaching, as applicants have previously discussed. The articles

only mention intramuscular injection in connection with regimens combining medroxyprogesterone acetate (MPA) and testosterone enanthate. With respect to all other progestagens used, only oral administration is suggested. Further, each of the articles which discuss intramuscular injection point out the disadvantages of such method, both in effectiveness and patient acceptance, i.e.:

- Alvarez-Sanchez et al, 1979 (Int J Androl, 2, pp. 136-149) conclude that this treatment schedule is not adequate for contraceptive purposes (see abstract).
- "none of the regimens reviewed here appear suitable for further development as a male contraceptive" (1st paragraph, column 2, page 709).
- Faundes et al, 1981 (Int J Andrology, 4, pp. 235-245) "the monthly schedule tried by us does not offer real promise of becoming a practical contraceptive for men, within a dose range free of potential toxicological effects. Perhaps other forms of administration can still be tried" (3rd paragraph, page 244).
- Frick et al, 1982, conclude that the treatment protocols (biweekly or monthly injections) proposed are inadequate for long term male contraception.

The Guerin article itself states: "The administration of steroids by injection has to disadvantages: (i) it is not well accepted by the subjects, and (ii) the plasma levels of steroids are not constant. Thus, Guerin focused on methods using oral administration "avoiding injections." See, e.g., the first two paragraphs on page 188 of Guerin.

Thus, it is urged that neither Guerin nor the articles it cites teach a method administering both a progestagen and an androgen, as defined in applicants' claims, wherein the androgen is particularly a testosterone ester which is administered by intramuscular injection, subcutaneous implantation, or subcutaneous injection. Further, although it makes a broad general statement regarding the alleged previous knowledge of administering both a progestagen and an androgen by intramuscular injection, it teaches one of ordinary skill in the art away from such methods. Unlike an anticipating disclosure, which can be applied in a rejection despite that the reference directs away from it (Celeritas Technologies Ltd. v. Rockwell International Corp., 47 USPQ2d 1516, 1522 (Fed. Cir. 1998)), a non-anticipating, broad generic disclosure does not support an obviousness rejection when the reference directs one of ordinary skill in the art away therefrom. A reference which "teaches away" from the claimed invention cannot render the invention obvious to one of ordinary skill in the art, see, e.g., Dow Chemical Co. v. American Cyanamid Co., 2 USPQ 2d 1350 (Fed. Cir. 1987); and, In re Dow Chemical Co., 5 USPQ 2d 1529 (Fed. Cir. 1988). For obviousness (even in view of a generic disclosure), the law requires motivation to one of ordinary skill in the art to arrive at the claimed invention. There is certainly no motivation in Guerin towards applicants' claimed invention since it disparages the previous intramuscular injection methods and has a goal of "avoiding injections."

For these reasons, Guerin, considered as a whole by one of ordinary skill in the art, does not teach or suggest a method of for suppressing spermatogenesis, inducing azospermia and/or inducing oligospermia in a male, by a method which includes intramuscular injection, subcutaneous implantation, or subcutaneous injection of a testosterone ester.

Regarding claims 191-194, 196-201, 206-209 and 214-216, Guerin also fails to disclose or suggest such a method wherein the administration is in intervals of not less than 6

weeks or is effective for at least 6 weeks. Guerin teaches, as its own contribution, only daily administration methods. The discussed prior art therein mentions bi-weekly and monthly interval administration methods but, not even in the general sense, administration methods of 6 weeks or more. Even for the bi-weekly and monthly methods discussed (i.e., Alvarez-Sanchez, Schearer, Faundes and Frick articles teaching intramuscular injection of medroxyprogesterone acetate (MPA) and testosterone enanthate), the references all teach that their methods are not adequate for male contraceptive purposes.

For all of the above reasons, it is urged that Guerin fails to render any of the above proposed claims obvious to one of ordinary skill in the art. Thus, the rejection under 35 U.S.C. §103 should be withdrawn.

For additional evidence of nonobviousness, applicants again refer to the data provided in the Kamischke article of record. The article shows that, upon selecting modified norethisterone as the progestagenic compound and a testosterone ester as the androgenic compound in male contraceptive regimens and selecting long-term intervals between intramuscular injection administration, significant suppression of sperm count in all participants occurs (page 532, col. 1, third paragraph). In the conclusive remarks on page 537-538 of Kamischke, it is stated that the “efficacy in all groups of the combination of TU (testosterone undecanoate) and norethisterone (norethisterone enanthate) has proven better than in nearly all other previous studies for hormonal male contraception.” Kamischke indicates that most potential users of male contraception would prefer an injection-independent application of the hormones, but except for the combination of norethisterone acetate with transdermal testosterone in a gel formulation, the injection or implantation-free approaches have failed so far to suppress spermatogenesis sufficiently (page 534, column 2, paragraph 1). This indication corresponds with the failure of the regimens investigated in the

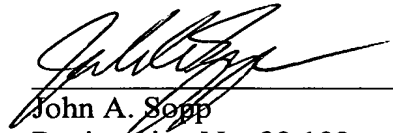
articles cited in Guerin (see the review of these articles above). This showing of unexpected advantages and patentability of the instant claims is very probative and convincing because the failure of the prior art methods is recognized in the articles relied on by Guerin. The showing demonstrates the advantages of the claimed invention as a selection invention within the broadly discussed previous intramuscular injection methods which Guerin (and the articles it cited) found disadvantageous and directed one of ordinary skill in the art away from. The showing of unexpected advantages in the Kamischke article is clear and convincing further evidence of the nonobviousness of the claimed invention.

For all of the above reasons, it is urged that Guerin, considered as a whole, fails to render the claimed invention obvious to one of ordinary skill in the art. Thus, the rejection under 35 U.S.C. § 103 should be withdrawn.

It is submitted that the claims are in condition for allowance. However, the Examiner is kindly invited to contact the undersigned to discuss any unresolved matters.

The Commissioner is hereby authorized to charge any fees associated with this response or credit any overpayment to Deposit Account No. 13-3402.

Respectfully submitted,



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